REMARKS

The following remarks are in response to the Examiner's Office Action mailed on March 11, 2004. Claims 23-80 have been canceled without prejudice. Claim 1 has been amended. Claims 1-22 are now pending. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

I. Specification

Applicants amend the Specification to correct a few editorial errors. No new matter has been introduced to the Specification .

II. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-22 stand rejected under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement. The Examiner bases the rejection on the court decision of *The Regents of the University of California vs. Eli Lilly and Company 119 F.3d 1559 (Fed. Cir., 1997)*. Specifically, the Examiner states that "the instant claims define the components of the claimed library only by their functional definition insufficient to adequately describe the claimed product." Applicants respectfully traverse the Examiner's grounds for rejection based on the following reasons.

Eli Lilly is inapplicable to the present claim of the invention. Under *Eli Lilly*, a claim lacks adequate written description if it is directed to **a nucleotide sequence** encoding a protein (e.g., human insulin) without providing the actual cDNA sequence in the specification. In contrast, Applicants claim **a library of nucleic acid constructs** each of which comprises i) a cis element sequence comprising one or more copies of a cis element to which a transcription factor is known to bind, the cis element sequence varying within the library of nucleic acid constructs; ii) a promoter sequence 3' relative to the cis element sequence; and iii) a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs. The cis element in each construct corresponds to a given reporter sequence within the library of nucleic acid constructs.

The Specification provides ample examples of what the library is and how to construct the library of nucleic acid constructs comprising various cis elements known to bind to various

transcription factors. Applicants respectfully direct the Examiner's attention to pages 13-16, a section under "DETAILED DESCRIPTION OF THE INVENTION", and Figures 1A, 1B, and 2. In particular, the table in Figure 2 lists numerous examples of cis elements (listed under the column labeled as "Cis-Element") that are known to bind to transcription factors (listed under the column labeled as "Transcription Factor"). The Specification further describes how to construct the library of nucleic acid constructs in the section entitled "Libraries Comprising Cis Element – Reporter Sequence Constructs", pp. 16-20.

According to the invention, one of the applications of the library of constructs is in rapid and efficient parallel identification of multiple different activated transcription factors in a biological sample. To identify the transcription factors in parallel, cis elements that are known to bind to different transcription factors are incorporated into a library of nucleic acid constructs. Meanwhile, a different reporter sequence is also incorporated into each member of the library to serve as a unique tag for each of the cis-elements. Figure 2 shows examples of the cis element (e.g., SEQ ID NO: 1) and examples of the reporter sequence (e.g., SEQ ID NO: 31) corresponding to the cis element listed in the column to its left side. Upon binding of the transcription factor to the cis element and activation of transcription, the cis element and its accompanying reporter sequence are transcribed. Because each cis element is tagged with a different reporter sequence, identification of the reporter sequence will lead to identification of the activated transcription factor that binds to the cis element. Page 13, lines 17-20.

In view of the detailed description and ample examples provided in the specification, Applicants submit that the claimed invention is adequately described to convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention under 35 U.S.C. §112, First Paragraph. Withdrawal of this ground of rejection is respectfully requested.

III. Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 1-22 under 35 U.S.C. §112, Second Paragraph as being indefinite. Applicants amend claim 1 to provide an antecedent basis for "the library of nucleic acid constructs." Applicants further amend claim 1 to specify that the reporter sequence is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library

of nucleic acid constructs. Applicants also amend claim 1 to clarify that since each cis element is tagged with a different reporter sequence, the cis element in each construct corresponds to a given reporter sequence within the library of nucleic acid constructs.

In view of these amendments to claim 1, Applicants respectfully request the Examiner to withdraw the rejection under 35 U.S.C. §112, Second Paragraph.

IV. Rejection Under 35 U.S.C. §102

Claims 1-13 and 20 stand rejected under 35 U.S.C. §102(b) as being anticipated by Kauffmann et al. (U.S. Patent No. 6,100,035).

Independent claim 1 as amended specifies a library of nucleic acid constructs each of which comprises i) a cis element sequence comprising one or more copies of **a cis element to which a transcription factor is known to bind**, the cis element sequence varying within the library of nucleic acid constructs; ii) a promoter sequence 3' relative to the cis element sequence; and iii) a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs. The cis element in each construct corresponds to a given reporter sequence within the library of nucleic acid constructs.

In contrast, Kauffmann et al. teaches a method of **identifying nucleic acid molecules that contain cis acting nucleic acid elements**. *See* Abstract. According to Kauffmann et al. the invention is to provide a solution to the problems existing in the art. Kauffmann et al. points out that "[a]t present... there is no broadly applicable method to identify cis acting nucleic acid elements **without prior identification of the regulated nucleic acid or of the regulatory nucleic acid binding factor**." Column 2, lines 4-7. To find cis acting nucleic acid elements in a diverse library of nucleic acid candidate molecules, a diverse population of nucleic acid molecules are used which comprise a plurality of different isolated polynucleotide nucleic acid molecules that **potentially** contain cis acting elements. Column 5, lines 59-64. Thus, this reference teaches a library of nucleic acid molecules some of which **might be** a cis element or cis elements after the screening assay. Therefore, Kauffmann et al. fails to teach the claimed library of nucleic acid construct each of which comprises one or more copies of **a cis element to which a transcription factor is already known to bind**.

Kauffman et al. also fails to teach a library of nucleic acid constructs each of which comprises a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs. Nowhere does this reference teach or suggest a library of nucleic acid constructs having a reporter sequence 3' relative to the promoter sequence which is 3' relative to the cis element. In support of the rejection based on Kauffmann et al's teaching of the claimed library having such reporter sequences, the Examiner directed Applicants' attention to the teaching in column 4, last paragraph and column 6, last two paragraphs. Upon careful review of these paragraphs, Applicants could not find either express or implicit teaching of such a library.

In view of the structural and functional distinction between the claimed invention and the disclosure of Kaufmann et al., Applicants submit that claims 1-22 are not anticipated by Kauffmann et al. under 35 U.S.C. §102(b). Withdrawal of this ground of rejection is therefore respectfully requested.

V. Rejection Under 35 U.S.C. §103

Claims 1-22 stand rejected under 35 U.S.C. §103(a) as being anticipated by Kauffmann et al. and Morris et al. (U.S. Patent No. 6,458,530).

As discussed in detail above, Kauffmann et al. fails to teach the claimed library of nucleic acid construct each of which comprises one or more copies of **a cis element to which a transcription factor is already known to bind**. On the other hand, Morris et al. teaches labeling and tracking cells and viruses by nucleic acid tags. *See* Abstract. Nowhere does Morris et al. teach or suggest a library of nucleic acid constructs each of which comprises i) a cis element sequence comprising one or more copies of a cis element to which a transcription factor is known to bind, the cis element sequence varying within the library of nucleic acid constructs; ii) a promoter sequence 3' relative to the cis element sequence; and iii) a reporter sequence that is 3' relative to the promoter sequence and comprises a variable sequence that varies within the library of nucleic acid constructs.

To establish a prima facie case of obviousness, the Examiner bears the burden of proving 1) the prior art reference (or references when combined) must teach or suggest all of the claim

limitations; 2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention; and 3) one of ordinary skill in the art at the time the invention was made would have reasonable expectation of success of the claimed invention. *In re Vaeck*, 947 F. 2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *In re O'Farrell*, 853 F. 2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); and *In re Dow Chem.*, 837 F. 2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

Kauffmann et al. teaches a method for identifying **new** cis elements from a diverse library of nucleic acid candidates. If a library of nucleic acid constructs each of which comprises one or more copies of a cis element to which a transcription factor is **already known** to bind, Kauffmann's purpose of finding new cis elements would have been defeated. Thus, the cited references not only fail to teach or suggest all of the claim limitations, but also fail to motivate one of ordinary skill in the art the modify the library in Kauffmann et al. in view of Morris et al. to arrive the claimed invention.

In view of the failure of the cited reference to teach or suggest the claimed invention, a prima facie case of obviousness has not been established under 35 U.S.C. §103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

CONCLUSION

In light of the remarks and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

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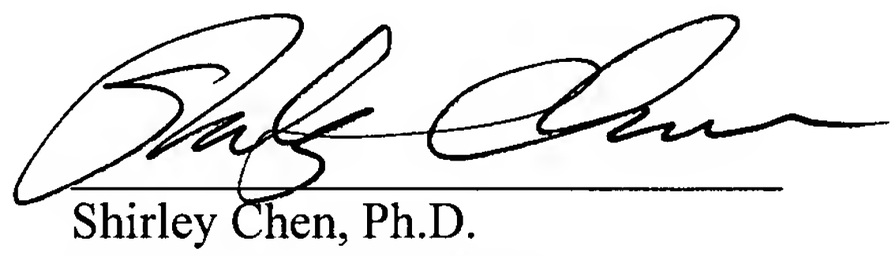
Respectfully submitted,

Date: July 28, 2004

By: 
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